XCII.—*The Oxime of Mesoxamide and some Allied Compounds.*

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BY the action of nitrosyl chloride on malonamide a substance is obtained which is characterised by the intense violet coloration it gives when mixed with ferrous sulphate and an alkali (Tilden and Forster, Trans., 1895, **67**, 490).

This substance can be prepared by the action of liquid nitrosyl chloride on malonamide in sealed tubes at the ordinary temperature. After several days there is evidence of considerable pressure, for, on opening the tubes, hydrogen chloride escapes together with unchanged nitrosyl chloride. It was more conveniently prepared, however, by passing a current of gaseous nitrosyl chloride through chloroform in which malonamide was suspended. The gas was rapidly absorbed, but the amide was attacked very slowly at the ordinary temperature, and it was necessary to warm the liquid from time to time to about 45—50°; a brisk evolution of gas then occurred, and the liquid became colourless. The white, crystalline powder was filtered off, washed with chloroform, and spread on a clock glass to dry; it continued to evolve hydrogen chloride for some time.

The crude product thus obtained was readily soluble in water, and the concentrated solution decomposed with evolution of carbon dioxide when evaporated on a steam-bath. The aqueous solution was therefore allowed to evaporate in a vacuum over sulphuric acid, and the dry residue extracted repeatedly with boiling ethyl acetate. A small quantity of insoluble matter was left, which was found to be ammonium chloride. From the ethyl acetate solution, a white, crystalline powder was deposited, which gave very strongly the characteristic colour reaction with ferrous sulphate. After recrystallisation from ethyl acetate, the substance melted with decomposition at 187°. It is readily soluble in water or alcohol, forming acid solutions from which, by spontaneous evaporation, it crystallises in small, clear prisms. It is also soluble in boiling acetone, ethyl acetate, or acetic acid, crystallising from the last in well-developed prisms containing acetic acid, which is given up on exposure to the air, the crystals efflorescing. It is insoluble in benzene, ether, or light petroleum. The aqueous solution assumes a bright yellow colour on the addition of ammonia, soda, or potash. The substance contains no chlorine. After boiling with hydrochloric acid, it reduces Fehling's solution. It does not respond to Liebermann's test. On analysis:

0·0919 gave 26 c.c. moist nitrogen at 20·5° and 766·7 mm. N = 32·58.
0·0766 „ 21·5 c.c. „ „ „ 20° „ 768 mm. N = 32·45.
$C_3H_5O_3N_3$ requires N = 32·06 per cent.

In a molecular weight determination:

0·0981 in 23·93 acetic acid gave a depression 0·135°. Mol. wt. = 118·4.
0·1351 in 23·93 „ „ „ „ 0·187°. Mol. wt. = 117·7.
The molecular weight of $C_3H_5O_3N_3$ is 131.

The substance is therefore an oxime having the formula

$$(CO\cdot NH_2)_2C\colon N\cdot OH.$$

Acetyl Derivative, $(CO\cdot NH_2)_2C\colon N\cdot O\cdot CO\cdot CH_3$.—The oxime dissolved in acetic anhydride on warming, and from the solution bright, well-formed, prismatic crystals separated; these were filtered off, washed with acetic anhydride, and dried in a desiccator. The acetyl derivative melts, with decomposition, at 190°, and dissolves sparingly in cold, but readily in hot water, doubtless suffering hydrolysis, as the solution is coloured yellow by an alkali, and gives the characteristic violet coloration on the addition of ferrous sulphate. On analysis:

0·1473 gave 30·5 c.c. moist nitrogen at 17° and 767·65 mm. N = 24·28.
$C_5H_7O_4N_3$ requires N = 24·28 per cent.

Salts.—The acid character of the oxime is strongly marked. One hydrogen atom is readily replaced by metals, giving rise to salts which, with one or two exceptions, are of a bright yellow colour. The alkali salts are readily soluble in water, and are precipitated in the form of silky, yellow needles on the addition of alcohol to the solutions. The silver, lead, barium, and calcium salts are less soluble, and separate in a crystalline form from concentrated solutions.

The *silver* salt, $(CO\cdot NH_2)_2C\colon N\cdot OAg$, was analysed, with the following result:

0·1650, on ignition, gave 0·0744 Ag. Ag = 45·09.
$C_3H_4O_3N_3Ag$ requires Ag = 45·34 per cent.

The *potassium* salt, $(CO\cdot NH_2)_2C\colon N\cdot OK$, was prepared by adding excess of potash to the concentrated aqueous solution of the oxime, and precipitating the salt by the addition of alcohol, filtering, and washing with alcohol until free from alkali.

0 5652 gave 0·2905 K_2SO_4. K = 23·08.
$C_3H_4O_3N_3K$ requires K = 23·12 per cent.

Ferrous Potassium Salt, $(CO\cdot NH_2)_2\cdot C\colon N\cdot OK,[(CO\cdot NH_2)_2C\colon N\cdot O]_2Fe$.—The capacity of forming coloured salts is certainly the most striking property of the oxime. The characteristic violet coloration with ferrous sulphate and an alkali is due to the formation of a double salt, which is obtained in the form of small, well-defined prisms of a purple colour, with a green or bronze lustre when ferrous sulphate is added to a concentrated aqueous solution of the potassium, sodium, ammonium, barium, or calcium salt. For the purpose of analysis, the ferrous potassium salt was prepared by adding freshly made ferrous sulphate solution to a concentrated aqueous solution of the potassium salt, the crystalline precipitate being rapidly filtered, washed two or three times with cold water, in which it was very soluble, and dried in a desiccator. When dry, the salt is perfectly stable, but is rapidly decolorised when left exposed in the damp state.

0·1351 gave 0·0223 Fe_2O_3. Fe = 11·56.
0·4546 ,, 0·0732 Fe_2O_3 and 0·0787 K_2SO_4. Fe = 11·27; K = 7·77.
$(C_3H_4O_3N_3)_3KFe$ requires Fe = 11·54; K = 8·06 per cent.

The *ethyl* derivative, $(CO{\cdot}NH_2)_2C{:}N{\cdot}OEt$, could not be obtained by the action of ethyl iodide and sodium ethoxide on the oxime. It was prepared, however, by the action of ethyl iodide on the silver salt suspended in alcohol; the change took place readily on warming, silver iodide being precipitated and a yellow solution formed, which, after filtration, was evaporated to dryness, and the yellow, crystalline residue recrystallised from boiling ethyl acetate. The derivative was thus obtained in the form of minute, colourless octahedra melting at 150—151°. It dissolves readily in water, but suffers hydrolysis as the solution becomes yellow with alkalis, changing to violet on the addition of ferrous sulphate.

0·1092 gave 25·7 c.c. moist nitrogen at 20° and 769·1 mm. N = 27·28.
$C_5H_9O_3N_3$ requires N = 26·41 per cent.

Analyses of the oxime and certain of its metallic and alkyl derivatives having indicated that it is the isonitroso-derivative of malonamide, it was prepared by three other methods, which confirm this view of its constitution—namely, by the action of nitrous acid on malonamide, by the action of hydroxylamine on dibromomalonamide, and by the action of ammonia on ethyl isonitrosomalonate.

Action of Nitrous Acid on Malonamide.—The gases obtained by the action of nitric acid of sp. gr. 1·3 on white arsenic were passed into a supersaturated solution of malonamide kept cool by ice. When the precipitated malonamide had all passed into solution and the liquid had acquired a blue or green colour, the tube was gently warmed until evolution of nitrous fumes ceased and the solution was colourless; it was then cooled and the operation repeated. Finally, the solution was allowed to evaporate in a vacuum over sulphuric acid, and the hard, crystalline masses thus obtained were dried, ground to powder, and recrystallised from ethyl acetate. By this method, a yield of 40 per cent. of the theoretical was readily obtained.

Action of Hydroxylamine on Dibromomalonamide.—Dibromomalonamide, prepared by the action of bromine on malonamide (Freund, *Ber.*, 1884, **17**, 782), was suspended in an alkaline solution of hydroxylamine hydrochloride ($1\frac{1}{2}$ mols.) and warmed on the steam-bath for 48 hours. At the end of that time, all the dibromomalonamide had passed into solution, the liquid had a bright yellow colour, and one drop gave, with ferrous sulphate, an intense violet colour, indicating the presence of the oxime in considerable quantity. The compound was not isolated, however, owing to the difficulty of separating it from the mixture of sodium bromide and chloride.

Action of Ammonia on Ethyl Isonitrosomalonate.—When ethyl isonitrosomalonate was mixed with excess of ammonia solution of sp. gr. 0·925, heat was developed and a dark yellow solution formed. After standing for sixteen hours, the yellow crystalline deposit was removed by filtration, washed with alcohol, and dried. It was identified as the ammonium salt of the oxime of mesoxamide by its colour, crystalline form, solubility, and the formation of the dark violet crystals of the double salt on treatment with ferrous sulphate solution. The yield was 80 per cent. of the theoretical.

Action of Nitrous Acid on the Oxime.—In preparing the oxime by the action of nitrous acid on malonamide, it was noticed that a white precipitate of long, silky needles was frequently deposited in the rapidly cooled solution. This is a product of the action of nitrous acid on the oxime, for it can be prepared by adding an aqueous solution of nitrous acid to the oxime, or to its potassium salt rendered colourless by a drop of hydrochloric acid. The substance was separated by filtration, washed with water and alcohol, and dried in a desiccator. It melts with decomposition at 215—220°, is slightly soluble in cold, but readily soluble in boiling water, and dissolves readily in alkalis, forming pale yellow solutions from which it is reprecipitated in the crystalline form on the addition of hydrochloric acid. The alkaline solutions do not give a violet coloration with ferrous sulphate. After boiling with hydrochloric acid, the substance does not reduce Fehling's solution; hence it is not an oxime. For the purpose of analysis, a specimen was recrystallised from boiling water, washed with cold water and with alcohol, and dried in a desiccator.

0·094 gave 26·6 c.c. moist nitrogen at 21·5° and 750·8 mm. N = 31·75 per cent.

By heating the substance with caustic potash, and collecting the distillate in a known quantity of sulphuric acid, 0·4213 evolved ammonia equivalent to 0·2088 H_2SO_4. N as $NH_2 = 14·17$ per cent.

These results agree with the numbers calculated from the formula of a pseudonitrole, $(CO{\cdot}NH_2)_2C(NO){\cdot}NO_2$, which requires 31·82 per cent. of nitrogen and 15·91 per cent. of nitrogen as amidogen. It does not, however, possess the properties usually regarded as characteristic of a pseudonitrole, and it does not respond to Liebermann's test.

The substance appears to be dimorphous, crystallising in long, silky needles, or very bright, shining plates, according to the conditions; the former are thrown down from the mixture when it is rapidly cooled, the shining plates are deposited when the cooling is gradual. Moreover, the needles tend to pass into the other form on recrystallising from water, or on long standing in the mixture.

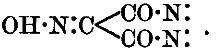
By the further action of nitrous acid on malonamide, ammonium quadroxalate and oxalic acid are formed and constitute the only solid products.

Reduction of the Oxime.—The oxime was readily reduced by the action of hydriodic acid on a concentrated aqueous solution in the cold. The liberated iodine was removed by shaking with mercury, and the excess of hydriodic acid by mercuric oxide. After removal of a trace of mercury from the solution by means of hydrogen sulphide, the liquid was evaporated to dryness, taken up with a little water, alcohol added until it produced turbidity, and the solution rendered clear by warming. Large, prismatic crystals associated with the cubical crystals of ammonium iodide were slowly deposited from the solution. The prismatic crystals, which consisted of the hydriodide of a base, blackened, but did not melt at 250°. On analysis:

0·1981 gave 0·1881 AgI. $I = 51{\cdot}30$.

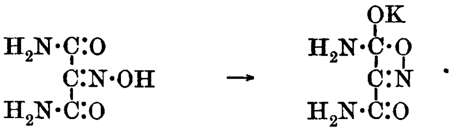
$C_3H_8O_2N_3I$ requires $I = 51{\cdot}78$ per cent.

The reduction product of the oxime is therefore *aminomalonamide*, $(CO{\cdot}NH_2)_2{\cdot}CH{\cdot}NH_2$, but the supply of material was too small to allow of the isolation of the base.

The capacity of forming red or purple alkali salts, and deep blue or violet ferrous salts, is characteristic of violuric acid, dimethylvioluric acid, isonitrosomalonylguanidine, and other ring compounds which contain the grouping  $OH{\cdot}N{:}C{<}\begin{matrix}CO{\cdot}N{:}\\ CO{\cdot}N{:}\end{matrix}$.

According to Hantzsch (*Ber.*, 1899, **32**, 594), the salts of violuric acid possess a constitution different from that of the acid, and involving transference of the hydroxyl from the oximido-group to the carbon atom of the adjacent carbonyl, and the subsequent linking of the nitrogen and the oxygen to form a four-membered ring.

The oxime of mesoxamide, although an open chain compound, also contains the characteristic grouping $OH{\cdot}N{:}C{<}\begin{smallmatrix}CO{\cdot}N{:}\\ CO{\cdot}N{:}\end{smallmatrix}$, and its formation of coloured salts may be due to a similar tautomeric change.



$$\begin{array}{l} H_2N{\cdot}C{:}O \\ \quad\ \ | \\ \quad\ \ C{:}N{\cdot}OH \\ \quad\ \ | \\ H_2N{\cdot}C{:}O \end{array} \longrightarrow \begin{array}{l} \qquad\ \ OK \\ \qquad\ \ | \\ H_2N{\cdot}C{\cdot}O \\ \quad\ \ |\ \ \ | \\ \quad\ \ C{:}N \\ \quad\ \ | \\ H_2N{\cdot}C{:}O \end{array}.$$

Oxime. Salt.

The only other substance which I have been able to find, having the property of giving a colour reaction with ferrous sulphate and an alkali, is isonitrosoguanidine, described by Thiele (*Annalen*, 1893, **273**, 133). It was at first thought that there might be some resemblance between this compound and those to which reference has just been made, and some isonitrosoguanidine was therefore prepared for purposes of comparison. Investigation showed, however, that the colour produced by alkalis does not differ markedly from that of the compound itself, whilst the shade obtained with ferrous sulphate is bluish-red and quite distinct from that produced with the oxime of mesoxamide. The constitution assigned by Thiele to isonitrosoguanidine seemed to exclude from consideration the possibility of its being the analogue of these oximes, but to put the question to the test of experiment the oxime of mesoxamethylamide (isonitrosomalonomethylamide), $OH{\cdot}N{:}C(CO{\cdot}NHMe)_2$, has been prepared by Andreasch's method (*Monatsh.*, 1895, **16**, 773). Contrary to Andreasch's experience, I find that the barium salt of this oxime is distinctly yellow. On the addition of ferrous sulphate to a solution of an alkali salt of this compound, a violet colour was obtained indistinguishable from that produced with the oxime of mesoxamide.

Further experiments are in progress to ascertain to what extent the colour reaction with ferrous sulphate is modified by the substitution of other radicles for the aminic hydrogen atoms in the oxime of mesoxamide.

The oxime of pyruvamide differs in constitution from that of mesoxamide in containing a CH_3 group in the place of one of the $\cdot CO\cdot NH_2$ groups of the latter; it was therefore expected that it would give similar, although modified, colour reactions. It was prepared by the action of ammonia on ethyl oximidopyruvate, and is a colourless, crystalline substance which melts at 176—177°, and dissolves sparingly in cold, but readily in hot water. It was recrystallised from boiling ethyl acetate. On analysis:

0·0921 gave 22 c.c. moist nitrogen at 20° and 768·8 mm. $N = 27{\cdot}66$.

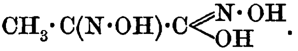
$C_3H_6O_2N_2$ requires $N = 27{\cdot}45$ per cent.

Alkaline solutions of this oxime exhibit no decided yellow colour, and the precipitate formed on the addition of ferrous sulphate is pale red, darkening rapidly to a deep reddish-brown.

The oxime of pyruvamide is described by Hantzsch and Urbahn (*Ber.*, 1895, 28, 760) as melting at 174—175°, and prepared by the joint action of ammonia and hydroxylamine on ethyl pyruvate. Two attempts were made to prepare the compound according to the instructions given, but without success; the only product isolated was an extremely soluble substance, extracted by ether from the mixture. On distilling off the ether, a yellow, syrupy liquid was left, which eventually solidified into a mass of pale yellow, prismatic crystals covered with a thin layer of a transparent, yellow solid; the two were identical in properties, readily soluble in water, alcohol, ethyl acetate, or acetone, but less soluble in ether, and insoluble in benzene, light petroleum, or chloroform. The aqueous solution gave a deep cherry-red colour with ferric chloride, and a green precipitate with copper acetate; the faintly yellow solution formed with alkalis became reddish-brown on the addition of ferrous sulphate, and threw down a precipitate. For the purpose of analysis, the substance was recrystallised from ether; the colourless, crystalline powder thus obtained melted with decomposition at 143°. The nitrogen in each of the two specimens was estimated:

0·1006 gave 20·7 c.c. moist nitrogen at 20·5° and 764·9 mm. N = 23·65.
0·1096 ,, 22·4 c.c. ,, ,, 21° ,, 763·6 mm. N = 23·38.
$C_3H_6O_3N_2$ requires N = 23·73 per cent.

The compound is, therefore, the hydroxamic acid of oximidopropionic acid,



$CH_3\cdot C(N\cdot OH)\cdot C\begin{smallmatrix} \nearrow N\cdot OH \\ \searrow OH \end{smallmatrix}$.

All attempts to prepare an isonitroso-derivative from succinamide by the action of nitrosyl chloride or nitrous acid were unsuccessful. Succinamide suspended in chloroform is not attacked by nitrosyl chloride; when sealed in a tube with liquid nitrosyl chloride for 7 days, it was partly converted to succinic acid. It was completely converted to succinic acid when treated with nitrous acid in water solution.

This work was undertaken at the suggestion of Professor Tilden, to whom my thanks are due for much help and encouragement during its progress.

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